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Long-term effect of inhaled colomycin on exercise capacity in adult patients with cystic fibrosis

G. Perpati[1], E. Pouliou[1], E. Stefanatou[1], V. Dionysopoulou[1], E. Armeniakou[1], S. Papakostopoulos[1], E. Christodoulou[2], A. Papamichalopoulos[2], S. Nanas[2], Ch. Roussos[2]
[1]*Cystic fibrosis Outpatient Clinic, Athens Chest Hospital,* [2]*Department of Pulmonary and Critical Care Medicine, National and Kapodistrian University, Athens, Greece*

INTRODUCTION: Exercise capacity in cystic fibrosis (CF) patients depends on infection control.
AIM: The aim of this study was to explore the effect of colomycin on exercise capacity and clinical status in adult patients with CF.
PATIENTS-METHODS: Fourteen patients with CF (6 male aged 21.1±12, and 8 female aged 24±8) were studied. They had FEV_1=45±33% pred. and SS=55±14. All patients were in stable state treated with rhDNAse and inhaled tobramycin in repeated cycles of 28 days on drug and 28 off drug. Patients underwent a CPET on a treadmill before and after treatment with colomycin (2000000 IU × 2 id for 6 months). Colomycin was given to patients on months they didn't receive tobramycin. Peak oxygen consumption (VO_2 peak) during CPET and at early recovery (VO_2 /t slope) were estimated.
RESULTS: Statistical analysis showed improve in SS (59.2 ± 9 before vs 68.3±11.7 after treatment, p<0.002), in VO_2 peak (18.3±5.7 vs 19,2±8.1, p<0.002) and VO2/t slope (0.41±0.2 vs 0.48± 0.31, p<0,007).
CONCLUSION: Inhaled Colomycin added to conventional therapy in adult patients with CF improves clinical status and exercise capacity.

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10 Years of Colistin use in a Regional Cystic Fibrosis Centre

I. Clifton[1], M. Denton[2], C. Etherington[1], D. Peckham[1], S. Conway[1]
[1]*Regional Adult Cystic Fibrosis Centre, Seacroft Hopsital,* [2]*Dept of Microbiology, Leeds General Infirmary*

Aims The aim of this study was to see if the wide spread use of intravenous (IV) colistin over a ten year period had resulted in an increase in the prevalence of colistin resistant isolates of Pseudomonas aeruginosa (PA) in patients with cystic fibrosis (CF).
Methods Data including the number of IV courses, antibiotics administered and PA antibiotic resistance were collected from the regional CF unit and microbiology databases between 1st Jan 1995 and 31st Dec 2004. Prior to 2000, antibiotic resistance testing was undertaken using a standardized disk diffusion technique, after this date the Stokes comparative disc diffusion method was used.
Results

	% Patients with colistin resistant PA isolate	Number of IV colisitin courses (Total IV courses)
1995	0.13%	213 (361)
1996	0.04%	211 (445)
1997	0.93%	240 (481)
1998	0.74%	273 (474)
1999	1.68%	365 (593)
2000	0.17%	306 (585)
2001	0.36%	297 (579)
2002	0.12%	306 (605)
2003	0.41%	174 (344)
2004	1.03%	230 (544)

Over the ten year study period, a mean of 0.70% and 0.42% patients before and after the year 2000 had a colistin resistant isolate of PA respectively. A mean of 477.7 IV antibiotic courses were administered annually. The mean number of IV course of colistin administered was 255.6 per year. Using linear regression the rate of increase in colistin resistance was 0.38% per year from 1995 until 1999. From the year 2000, the rate of increase was 0.18% per annum.
Conclusions Direct comparison of resistance data before and after the year 2000 can not be made as two different laboratory techniques were used to assess resistance. However our results show that despite the frequent use of IV colistin, there has been little change in the prevalence of colistin resistance among isolates of PA over a ten year period.

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Experiences from 15 years use of inhaled colistin in treatment of *P. aeruginosa* in a CF-clinic

C.R. Hansen[1], T. Pressler[2], N. Høiby[1]
CF-Centre, Departments of [1]*Microbiology and* [2]*Paediatrics, Rigshospitalet, Copenhagen, Denmark*

Aim/method: Since 1989, intermittent colonization with *P. aeruginosa* has been treated with inhaled colistin and oral ciprofloxacin. The aim of this study is to assess the effect of this treatment strategy on the occurrence of PA strains resistant to colistin. A population of CF-patients without chronic PA infection were followed for 15 years. 146 patients were included.
Results: Median age at time of diagnosis of CF was 0.5 years (range 0 – 12). The study period includes 1871 patient-years. Intermittently colonized patients had a median number of 5 (range 1 – 46) sputum samples with growth of PA, resulting in a total number of 1052 treatments. Treatment-length changed during the study period from initially 3 weeks courses to, in the late 1990´s, 3 months courses. 39 patients (27%) developed chronic PA-infection. Median age at onset of chronic infection was 14.5 years (range 3.6 – 28.3). All chronically infected patients have been treated with inhaled colistin continuously.
We investigated 1052 sputum samples positive for PA, collected from intermittently colonized patients, and 3870 sputum samples positive for PA from chronically infected patients. Among chronically infected patients, only 4 patients (14 sputum samples) had growth of colistin-resistant strains of PA at some time. (0.4% of strains from chronically infected patients, 0.3% of all isolated strains). These patients had been chronically infected for 2, 4, 8 and 9 years, respectively. No intermittently colonized patients had growth of colistin-resistant strains.
Conclusion: Of 146 patients with intermittent *P. aeruginosa* infection, 39 became chronically infected during a study period of 15 years. 4 chronically infected patients had transient colonization with colistin-resistant strains.

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In-vitro based comparison of deposition efficiency of two inhalation systems for inhalation of Colistin

B. Müllinger[1], P. Brand[2], O. Pechtold[2], K. Sommerer[2], G. Scheuch[1]
[1]*Inamed GmbH, 35285 Gemünden,* [2]*Inamed Research GmbH & Co. KG, 82131 Gauting, Germany*

Inhalation of Colistin is an important intervention in the therapy of patients with cystic fibrosis. In order to improve inhalation of Colistin (3ml, Grünenthal), this in-vitro study was performed with a conventional nebulizer (Pari Turbo Boy N/Pari LC Plus) and an inhalation system that controls the breathing pattern during inspiration (AKITA/Pari LC Star).
In this study, two different techniques and devices to administer inhaled Colistin were compared. The first device is conventionally used for Colistin inhalation (Pari LC Plus® with Pari Turbo Boy N® compressor), while the second device uses a jet nebulizer (Pari LC Star®) in combination with an "intelligent" compressor (Akita®) to control the breathing pattern. Emitted dose and particle size were measured and used to estimate lung deposition using the ICRP-lung deposition model. The time necessary to deposit a fixed amount of drug in the lung was also evaluated.
Results: In-vitro measurements and deposition calculations.

Nebulizer System	MMD [µm]	Emitted Dose [ml]	Time for depositing 0.46 ml within the lungs [min]	Maximum Deposition within the lungs [ml]
LC PLUS + TURBO BOY	3.60	32.6	6.1	0.46
LC STAR +AKITA	2.82	63.9	4.2	1.65

In this in-vitro study is has been shown that the inhalation of Colistin using controlled breathing pattern with the AKITA® system results in more efficient drug delivery compared to the conventional inhalation system PARI Turbo Boy N® / LC Plus®. Using the AKITA® device, drug nebulization only takes place during the inspiration period whereas with the conventional device, nebulization is continuous, resulting in a considerable drug loss during the expiration phase. Second, the AKITA® device uses a controlled deep and slow inhalation pattern.